1 Medical Research Council. Treatment of acute lymphoblastic leukaemia: effect of "prophylactic" therapy against central nervous system leukaemia. *Br Med J* 1973;ii:381-4.
2 Campbell RHA, Marshall WC, Chessells JM. Neurological complications of childhood leukaemia. *Arch Dis Child* 1977;52:850-8.
3 Medical Research Council. Effects of varying radiation schedule, cyclophosphamide treatment, and duration of treatment in acute lymphoblastic leukaemia. *Br Med J* 1978;ii:787-91.
4 Hustu HO, Aur RJA, Verzosa MS, Simone JV, Pinkel D. Prevention of central nervous system leukemia by irradiation. *Cancer* 1973;**32**:585-97.
5 Moe PH, Seip M, Finne PH. Intermediate dose methotrexate (IDM) in childhood acute lymphocytic leukemia in Norway. *Acta Paediatr Scand* 1981;**70**:73-9.
6 Sullivan MP, Chen T, Dyment PG, Huizdala E, Steuber CP. Equivalence of intrathecal chemotherapy and radiotherapy as central nervous system prophylaxis in children with acute lymphatic leukemia: a pediatric oncology group study. *Blood* 1982;**60**:948-58.
7 Soni SS, Marten GW, Pitner SE, Duenas DA, Powazek M. Effects of central nervous system irradiation on neuropsychologic functioning of children with acute lymphocytic leukemia. *N Engl J Med* 1975;**293**:113-8.
8 Maguire P, Comaroff J, Ramsell PJ, Jones PHM. Psychological and social problems in families of children with leukaemia. In: Jones PHM, ed. *Topics in paediatrics I. Haematology and oncology*. Tunbridge Wells: Pitman Medical, 1979:141-9.
9 Eiser C, Lansdown R. Retrospective study of intellectual development in children treated for acute lymphoblastic leukaemia. *Arch Dis Child* 1977;52:525-9.
10 Eiser C. Effects of chronic illness on intellectual development. A comparison of normal children with those treated for childhood leukaemia and solid tumours. *Arch Dis Child* 1980;55:766-70.
11 Moss HA, Nannis ED, Poplack DG. The effects of prophylactic treatment of the central nervous system on the intellectual functioning of children with acute lymphocytic leukemia. *Am J Med* 1981;**71**:47-52.
12 Jannoun L. Are cognitive and educational development affected by age at which prophylactic therapy is given in acute lymphoblastic leukaemia? *Arch Dis Child* 1983;**58**:953-8.
13 Meadows A, Gordon J, Massari DJ, Littman P, Fergusson J, Moss K. Declines in IQ scores and cognitive dysfunctions in children with acute lymphocytic leukaemia treated with cranial irradiation. *Lancet* 1981;ii:1015-8.
14 Rowland JH, Glidewell OJ, Sibley RF, *et al*. Effects of different forms of central nervous system prophylaxis on neuropsychologic function in childhood leukaemia. *Journal of Clinical Oncology* 1984;2:1327-35.
15 Esseltine DW, Freeman CR, Chevalier R, *et al*. Computed tomography brain scans in long term survivors of childhood acute lymphoblastic leukemia. *Med Pediatr Oncol* 1981;**9**:429-38.
16 Ochs JJ, Parvey LS, Whitaker JN, *et al*. Serial cranial computed tomography scans in children with leukemia given two different forms of central nervous system therapy. *Journal of Clinical Oncology* 1983;1:793-8.
17 Shalet SM, Beardwell CG, Pearson D, Morris-Jones PH. The effect of varying doses of cerebral irradiation on growth hormone production in childhood. *Clin Endocrinol* 1976;5:287-90.
18 Ahmed SR, Shalet SM. Hypothalamic growth hormone releasing factor deficiency following cranial irradiation. *Clin Endocrinol* 1984;**21**:483-8.
19 Shalet SM, Beardwell CG, Twomey JA, Jones PHM, Pearson D. Endocrine function following the treatment of acute leukemia in childhood. *J Pediatr* 1977;**90**:920-3.
20 Shalet SM, Price DA, Beardwell CG, Jones PHM, Pearson D. Normal growth despite abnormalities of growth hormone secretion in children treated for acute leukemia. *J Pediatr* 1979;**94**:719-22.
21 Deeg J, Storb R, Thomas ED. Bone marrow transplantation: a review of delayed complications. *Br J Haematol* 1984;57:185-208.
22 Nesbit ME, Sather HN, Robison LL, *et al*. Presymptomatic central nervous system therapy in previously untreated childhood acute lymphoblastic leukaemia. Comparison of 1800 rad and 2400 rad. *Lancet* 1981;i:461-5.

Phantom pregnancy

Pseudocyesis is a condition in which a non-pregnant—and non-psychotic—woman firmly believes herself to be pregnant and develops objective signs of pregnancy.[1] Most cases are said to occur between the ages of 20 and 39, though the age range in one series was 5-79,[2] and cases have recently been described in teenagers.[3-5] The most common symptom is amenorrhoea or oligomenorrhoea, usually for nine months.[6] There is also abdominal enlargement, but without effacement of the umbilicus. Breast changes, which occur in 80% of patients,[2] include tenderness and swelling, secretion of milk or colostrum, and areolar pigmentation. Patients often claim to feel fetal movements, usually earlier than in a genuine pregnancy.[1] There may be vomiting, morning nausea, aberrations of appetite, and weight gain, and a case of "toxaemia" has been reported.[6] The diagnosis may be difficult,[7] but nowadays should easily be made with the help of ultrasound.[8] Occasional cases have been described in men,[2 9] but these may be associated with psychosis or organic disease.[9]

Phantom pregnancy was first described by Hippocrates and has since affected all races and strata of society, including British royalty, American slaves, and Chinese coolies.[2] It seems to be becoming rarer,[1 2] partly because increasing diagnostic accuracy means that it is no longer confused with conditions like hyperprolactinaemia, partly because in developed countries there is less pressure on women to become pregnant, and partly because of increasing public knowledge about medical matters. Nevertheless, the incidence is still comparatively high among black people in Africa,[10 11] and in developed countries immigrants may remain at risk.[3-5 12] Patients are usually naive about medical matters,[13] and may have either a strong desire for pregnancy or a fear of conceiving.[14] The condition may be a form of hysterical conversion,[3] or depression may be present.[1 6 14] A "pregnancy" may help a woman cope with distress or loss,[6 15] and an association with child stealing has been reported.[12]

What is the endocrine mechanism of pseudocyesis? In laboratory rats pseudopregnancy may be induced by various means, including genital stimulation,[2 16] and is due to persistence of a corpus luteum in the absence of pregnancy; neurogenic suppression of prolactin inhibitory factor may occur, allowing prolactin to help maintain the corpus luteum.[17] In human pseudocyesis, however, a corpus luteum is often absent[2 17] and the basal plasma prolactin concentration may be normal[18 19] or raised.[5 17] Basal plasma concentrations of follicle stimulating hormone are normal,[5 17-19] while the luteinising hormone value may be normal[17-19] or raised.[5] The pulsatile pattern of luteinising hormone and prolactin secretion is exaggerated,[5] and administration of luteinising hormone releasing hormone and thyrotrophin releasing hormone produces exaggerated responses of luteinising hormone and prolactin respectively.[17-19] In a recent study of five patients in Florida the gonadotrophin concentrations were within the normal range but luteinising hormone was consistently higher than follicle stimulating hormone, while prolactin and progesterone were mildly increased.[13] Apart from the raised progesterone value this pattern is similar to that in polycystic ovary disease.

In some types of amenorrhoea—particularly hyperprolactinaemic amenorrhoea—there are increased concentrations of opioid peptides (endorphins). These inhibit pulsatile release of luteinising hormone,[20] and thus administration of the opioid antagonist naloxone to these women stimulates release of luteinising hormone. Since opioid peptides may influence behaviour as well as hormone concentrations it was suggested that their production might be increased in pseudocyesis; but when naloxone was given to women with pseudocyesis it failed to induce release of luteinising hormone or prolactin.[13] After the patients were told their diagnosis, however, the naloxone response appeared to return to normal. This suggests that pseudocyesis is not associated with increased opioid activity, though possibly there may be a reduction in tonic opioid inhibition.

Treatment usually entails confronting the patient with the diagnosis.[15] Normally when this is done hormone concentrations return to normal quickly, the abdominal distension begins to disappear,[5] and there may even be a rapid drop in weight.[21] Nevertheless, patients may resist the diagnosis,[1 7] and once they realise the truth depressive illness may occur.[7] Recurrence is common,[2 4 14] and close cooperation between gynaecologist and psychiatrist is important.[7] Psychotherapy[2 14 15] and family therapy[4] may be necessary, and appropriate follow up is essential.[14 21]

JAMES OWEN DRIFE

Senior Lecturer in Obstetrics and Gynaecology,
University of Leicester,
Leicester LE2 7LX

1 Murray JL, Abraham GE. Pseudocyesis: a review. *Obstet Gynecol* 1978;51:627-31.
2 Cohen LM. A current perspective of pseudocyesis. *Am J Psychiatry* 1982;**139**:1140-4.
3 Hardwick PJ, Fitzpatrick C. Fear, folie and phantom pregnancy: pseudocyesis in a fifteen-year-old girl. *Br J Psychiatry* 1981;**139**:558-62.

4 Rosenberg HK, Coleman BG, Croop J, Granowetter L, Evans AE. Pseudocyesis in an adolescent patient. *Clin Pediatr* 1983;**22**:708-12.
5 Yen SSC, Rebar RW, Quesenberry W. Pituitary function in pseudocyesis. *J Clin Endocrinol Metab* 1976;**43**:132-6.
6 Brown E, Barglow P. Pseudocyesis: a paradigm for psychophysiological interactions. *Arch Gen Psychiatry* 1971;**24**:221-9.
7 Christodoulou GN. Pseudocyesis. *Acta Psychiatr Belg* 1978;**78**:224-34.
8 Guzinski GM, Conrad SH. Pseudocyesis and sonography. *Am J Obstet Gynecol* 1980;**138**:230-2.
9 Evans DL, Seely TJ. Pseudocyesis in the male. *J Nerv Ment Dis* 1984;**172**:37-40.
10 Brenner BN. Pseudocyesis in blacks. *S Afr Med J* 1976;**50**:1757-9.
11 Osotimehin BO, Ladipo OA, Adejuwon CA, Otolorin EO. Pituitary and placental hormone levels in pseudocyesis. *Int J Gynaecol Obstet* 1981;**19**:399-402.
12 d'Orban PT. Child stealing and pseudocyesis. *Br J Psychiatry* 1982;**141**:196-8.
13 Devane GW, Vera MI, Buhi WC, Kalra PS. Opioid peptides in pseudocyesis. *Obstet Gynecol* 1985;**65**:183-8.
14 Zuber T, Kelly J. Pseudocyesis. *Am Fam Physician* 1984;**30**(5):131-4.
15 Weddington WW, Porter SG. Pseudocyesis following sterilization: role of the pseudofather. *Psychosomatics* 1984;**25**:563-5.
16 Luque EH, Castro-Vazquez A. Sensory mechanisms involved in the induction of pseudopregnancy by progesterone: increased sensitivity to stimulation of the pudendal sensory field. *Endocrinology* 1983;**113**:385-90.
17 Zarate A, Canales ES, Soria J, Jacobs LS, Daughaday WH, Kastin AJ, Schally AV. Gonadotropin and prolactin secretion in human pseudocyesis. *Ann Endocrinol (Paris)* 1974;**35**:445-50.
18 Tulandi T, McInnes RA, Lal S. Altered pituitary hormone secretion in patients with pseudocyesis. *Fertil Steril* 1983;**40**:637-41.
19 Tulandi T, McInnes RA, Mehta A, Tolis G. Pseudocyesis: pituitary function before and after resolution of symptoms. *Obstet Gynecol* 1982;**59**:119-21.
20 Grossman A, Rees LH. The neuroendocrinology of opioid peptides. *Br Med Bull* 1983;**39**:83-8.
21 Starkman MN. Impact of psychodynamic factors on the course and management of patients with pseudocyesis. *Obstet Gynecol* 1984;**64**:142-5.

Regular Review

Clinical management of benzodiazepine dependence

ANNA C HIGGITT, M H LADER, P FONAGY

The development of dependence after the long term use of benzodiazepines is now supported both by clinical evidence and by the results of double blind studies.[1-3] Withdrawal symptoms have been reported after treatment for as little as four to six weeks.[4,5] The withdrawal symptoms observed are wide ranging, and, while they include some related to anxiety, they are clearly distinguishable from a simple re-emergence of pre-existing anxiety.[6-8] Particularly frequently reported are instances of increased sensory perception such as hyperacusis, photophobia, paraesthesiae, hyperosmia, and hypersensitivity to touch and pain, but gastrointestinal disturbances, headaches, muscle spasms, vertigo, and sleep disturbances are also frequent.[3,9,10] The proportion of long term users of benzodiazepines in whom withdrawal symptoms may be expected to emerge has been variably estimated to be between 15% and 44%.[3,8] The symptoms typically emerge in the first week after stopping the drug but may develop after a reduction in dosage.[7,10] Until recently the withdrawal syndrome was reported as lasting for up to three months,[7] but we are now seeing more patients whose symptoms have persisted for more than six months—in some cases for a year or more.

Yet no one doubts that most patients currently taking benzodiazepines should stop them. One and a quarter million of the British population take benzodiazepines for more than a year,[11] although data supporting their continued effectiveness over such a period are sparse—to say the least.[12] A recent review concluded that benzodiazepines are no more effective than brief counselling by the general practitioner for the common minor affective disorders and that their prescription should be cut.[13] There is, in addition, evidence suggesting possible psychological impairment and neuroradiological changes associated with long term administration.[14,15] Recent extensive publicity about tranquillisers has led to an increased consumer demand for medical guidance about withdrawal.[16] Information on optimal withdrawal procedures is lacking—for little systematic research has been done on the treatment of benzodiazepine dependence,[6] and the studies that have been published have had methodological limitations.[17] The guidelines set out below are based in part on a review of published work and also experience in our unit in withdrawing more than 60 patients over the past seven years.

Setting

In general withdrawal is best tackled in the outpatient setting.[2,9] Patients having high doses or with a history of seizures or psychotic episodes during previous attempts at withdrawal are more safely treated as inpatients.

Rate of withdrawal

Stopping the drug abruptly is more likely to lead to severe withdrawal symptoms such as fits or confusional states[18,19]—and to loss of patients from the withdrawal programme.[3] No consensus exists, however, on the precise duration of the withdrawal process or the size of each reduction in dosage. Four weeks is probably the minimum period,[1,2,9] and programmes as long as 16 weeks have been recommended.[20] Over the withdrawal period dosage should gradually be tapered off in steps ranging from 0·5 to 2·5 mg diazepam or its equivalent.[3,4,7,12,21] The table sets out equivalent doses for benzodiazepines on the limited list.

Some patients referred for withdrawal of benzodiazepines may already be complaining of withdrawal symptoms.[10] Published reports tend, however, to emphasise patients who had severe problems in withdrawing and so need appraisal by specialists. Some and possibly most patients will suffer less severe withdrawal symptoms and will cope well with a fairly rapid reduction in dosage over a few weeks.[22]

In our view—and certainly for patients who have previously had problems withdrawing—the rate of reduction of dosage should not be fixed at the outset but should be "titrated" against the patient's withdrawal symptoms.